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(54) **Coated stent**

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Description

The present invention relates to a coated stent, in particular to a biocompatible polymer-coated stent and to a process for the manufacturing thereof.

Stenosis resolution of cylindrically-shaped hollow biological structures, such as circulatory system vessels, esophagus, bile ducts, intestine, urinary tracts and respiratory tract, at present have several possibilities offered by surgery, endoscopy, radiology.

Sometimes the pathological entity does not allow surgical practice, in this case endoscopic operation or radiologic intervention are practised for palliative and/or curative purpose.

The use of stents, namely expandable devices which have the purpose to maintain the stenotic lumen patent, is a technique always in progress (K.C. Wright et al.; Radiology, 156:69-72,1985; J.C. Palmaz et al.; ibid., 164:705-708, 1987; G.K. McLean et al., ibid., 170:961-967, 1989).

Present uses of stents refer to the treatment of stenosis of bile ducts, arterial vessels, esophagus, urinary tracts and respiratory tract. Stents are also used in repair of aneurysms.

The mesh structure of stents, whilst on one hand allows their percutaneous application through catheters and ensures the mechanical characteristics that maintain the lumen patency, on the other hand puts some problems according to specific cases. In the event of a stent implant in a blood vessel, the stent structure may perturb haemodynamics, therefore increasing the risk of thrombus formation. If the stenosis is caused by neoplastic proliferation, ristenosis may occur after stent implant because of tumour cell infiltration through the meshes of the stent itself (Severini, Cozzi, Bellomi, Cigada, Tanzi; Biomateriali, 3/4 (1990) 79-84).

In most cases, stents are made of metallic materials, particularly stainless steel, titanium, or shape-memory alloys (Ni-Ti alloys). Said materials meet the structural and mechanical requirements, but involve some problems of biocompatibility and allergy, particularly when they come in contact with blood.

EP 0 480 667, in the name of Cook Inc., discloses a self-expanding percutaneous stent (Gianturco stent) covered by a flexible sleeve which is open at both ends. The flexible sleeve is welded or pinched at the ends of the stent. In the same reference, the possibility to coat the stent with plastic material is mentioned, but no specific teaching about the material nor the coating technique is provided.

Song et al., Radiology, 1991,; 180:349-354, describe a Gianturco stent wrapped with a nylon mesh coated by silicon rubber, for the palliative treatment of esophagogastric neoplasm obstructions.

The stent obtained by Song et al. involves two kinds of still unsolved problems: the difficult retrieval of the introducer sheath, due to the friction between stent coating (silicon rubber) and the sheath itself, and the anchorage of the stent to the esophagus mucosa, where the stent may be moved from by mechanical stresses, due to peristalsis.

Alvarado, Palmaz, et al. (Radiology, 1989, 170:975-978) describe polymer-coated balloon expandable stents and their application in bile ducts. The polymers used therein are silicon rubber and polyethere urethane.

EP 0518704 describes a temporary stent comprised of a plurality of metallic wires coated with polymeric material such as aliphatic polyurethane, silicone. The stent is particularly adapted to reduce the tendency to permanently adhere to the inner surface of the vascular walls.

To date there is still the need to provide coated stents with improved mechanical and biocompatibility characteristics.

It has now been found that coating a stent with a thermoplastic polycarbonate urethane, prostheses having excellent biomechanical characteristics for the treatment of stenosis and aneurysms are obtained. In particular, the inner surface of the polymer-coated stent is totally smooth, whilst the outer surface perfectly fits to the stent mesh structure. In this manner the so obtained stent presents the advantage of a smooth lumen surface, therefore a better fluid hydrodynamic, together with a structure having improved biomechanical characteristics. At the same time, the copolymer outer surf ace perfectly follows the development of the stent structure thus allowing an optimal interaction of the prosthesis with the lumen mucosa and the consequent non migration of the prosthesis itself from the implant site.

Several kind of biocompatible polymers are well-known, for example polyethyleneterephthalate, polytetrafluoroethylene (Teflon), polymethacrylates and various types of block copolymers belonging to the class of polyurethanes.

Polyether urethanes are known as suitable materials for implantable prosthesis, but have proved to be not very resistant to the attack by the biological environment where they are implanted (Pinchuck et al., 17th Annual Meeting of the Society for Biomaterials, 1991, Scottsdale, AZ, USA).

Therefore, it is an object of the present invention a polycarbonate urethane-coated stent and the coating process thereof.

The particular type of stent to be used in the present invention is not critical. Stents which are well-known to the man skilled in the art can be used, both self-expandable, and balloon-expandable, such as Palmaz, Palmaz-Schatz, Gianturco, Gianturco-Roubin, Gianturco-Rosch, Strecker and memory-shape stents.

A preferred embodiment of the present invention provides the use of a coated Gianturco-Rosch stent and the variations thereof.

The biocompatible copolymer to be used according to the present invention is a polycarbonate urethane of the type disclosed in US 5.133.742 (Pinchuck) and EP 0 461 375 (Corvita Corp.) and is marketed with the trade name Corethane(R).

According to the present invention, stent coating must take in consideration the desired final characteristics of the prosthesis and its use.

The stent may be coated either with a single copolymer layer or with more copolymer layers.

A further object of the present invention is a process for coating a stent, said process comprising the steps of:

a) positioning the stent in its expanded configuration on a horizontal rotating bearing;
b) rotating said bearing;
c) deposition of the copolymer on said stent while rotating;
d) removing the coated stent from said rotating bearing.

In a typical embodiment of the present invention, the stent is put on a bearing made of a suitable material, Teflon for example, then the bearing is rotated at a definite speed and a copolymer solution is deposed on the stent to be coated.

The copolymer is dissolved in a suitable organic solvent, such as dimethylacetamide, dimethylformamide, at a concentration ranging from 10 to 40% w/w, preferably from 15 to 20%. Maximum bearing rotating speed is 20 rpm.

The following examples further illustrate the invention.

EXAMPLE 1

A segmented thermoplastic polycarbonate urethane (Corethane(R)) was used to coat a Gianturco-Rosch stent.

To this end, 10 g of Corethane(R) 80A, commercially available as 44.84% w/w solution, were added with 16.37 g of dimethylacetamide (DMAC), obtaining 26.37 g of a 17% Corethane(R) solution.

The solution was left in a thermostatic bath at 70-75°C under stirring for about 5-10 hours and subsequently at room temperature.

Two Gianturco-Rosch stents, one single-body stent having 8 mm diameter (stent A) and one double-body stent having 7 mm diameter (stent B) were used.

To carry out the coated stent, a horizontal shaft electric motor, rotating at the speed of 2 rpm, was used, wherein a teflon cylindric bearing having a diameter equal to the stent diameter, was mounted by means of a coupling gear. The stent was inserted on the cylindric bearing, the latter was fixed on the motor shaft and the rotation of the device was started.

The polymeric material solution was dropped by means of a pipette on the rotating metallic grid till complete coating of the device.

The device was kept rotating in a fume hood for 24 hours till complete solvent evaporation. The stent was removed from the mandrel using distilled water as detaching agent. A stent coated with a copolymer monolayer of a thickness of about 0.1 mm was obtained.

EXAMPLE 2

According to the process described in Example 1, two Gianturco-Rosch stents, the same as the above ones, were coated using a polyether urethane known under the trade name Pellethane (R) 2363 80A by Dow Chemical.

EXAMPLE 3

In this Example the mechanical characteristics of the coated stent according to the invention (Example 1) compared with stents coated with another kind of polyurethane are illustrated.

External pressure stiffness tests

This test intends to evaluate the stent stiffness to an external pressure. The importance of such a test stands in that the stent in working conditions undergoes to an external pressure by the vessel or duct wall, which could decrease the lumen, thus lowering the device efficacy.

To carry out the tests, a device simulating the effect of a pressure exerted by a biological wall was carried out. Said device consists of two elements. The former is a rectangular plexiglas bearing (3x2.5 cm) wherein a slot (2x21mm) was obtained. The latter is an inextensible cloth ribbon. The ribbon is inserted in the plexiglas bearing forming an eyelet wherein the tested device is inserted.

By fixing the ribbon ends to the clamps of a microdynamometer it is possible to evaluate the strength necessary to determine a reduction of the stent diameter. The test was carried out both on coated stents and on the corresponding uncoated ones (stent C and D).

The results show that the coated stents have a higher stiffness to an external pressure than the uncoated stents, as shown in Table 1 below.

TABLE 1

Strength necessary to decrease diameter.				
DIAMETER DECREASE (mm)	STRENGTH (N)			
	Stent A	Stent C	Stent B	Stent D
1	0.88	0.14	0.72	0.63
2	2.84	0.22	2.96	1.15
3	7.78	0.40	6.96	2.03
4	8.50	0.64	11.08	3.70

Adhesion test

Adhesion test intends to compare adhesion ability of the two polymer materials to the stent metallic structure (AISI 316 stainless steel). The choice of this test comes from the observation that better adhesion ability between polymeric material and metal tends to minimize the problems linked to the stent insertion in the catheter and its release in the biological environment. Accordingly, the results of said test are deemed to provide useful informations about the better metal-polymer matching.

The test was carried out according to ASTM C 794-80.

Sample preparation

The above described polymer solution was poured into cylindrical molds sealed on a glass plate; 2 mm wide-metal stripes (AISI 316 stainless steel) were immersed in the molds.

The molds containing the solution and the steel stripes were put in a vacuum oven at 70°C for 24 hours.

After complete solvent evaporation, samples, wherein part of the metal stripe was completely immersed in the polymeric material, sizing 5.4x20 mm, were thus obtained.

The instrument used for the tests was a microdynamometer (Minimat, Polymer Laboratories). Tests were carried out at a clamp separation speed of 3 mm/min till detachment of metal from polymer material.

The results are shown in Table 2 below.

TABLE 2

Adhesion test of Corethane(R) and Pellethane (R) to stainless steel AISI 316.		
	Corethane	Pellethane
Disjunction stress (MPa)	0.43	0.34
	0.53	0.28
	0.50	0.26
	0.32	0.32
	0.54	0.40
	0.29	0.25
	0.31	0.31
	0.24	0.29
Mean	0.40	0.31
Std. Dev.	0.12	0.05

EXAMPLE 4

In this example the resistance of the coated stents according to the present invention to the biological environment, in the present case prolonged contact with bile, was assayed. Bile was withdrawn from patients suffering from extraepatic bile duct obstruction and contacted with coated stents according to the present invention.

After 1 month of contact, no bile deposits were observed on the polymer coating.

Claims

1. A coated metal stent, characterized in that said stent is coated with a thermoplastic polycarbonate urethane, and in that the inner surface of the polymer-coated stent is totally smooth, whilst the outer surface perfectly fits to the stent mesh structure.

2. A stent according to claim 1, wherein Corethane(R) is the polycarbonate urethane.

3. A stent according to claims 1-2, wherein said stent is selected from the group consisting of Palmaz, Palmaz-Schatz, Gianturco, Gianturco-Roubin, Gianturco-Rosch, Strecker, memory-shape stent.

4. A stent according to claims 1-3, wherein a Gianturco-Rosch is said stent.

5. A process for coating a stent of claims 1-4, said process comprising the steps of:

   a) Positioning the stent in its expanded configuration on a horizontal rotating bearing;
   b) Rotating said bearing;
   c) Deposition of the copolymer on said stent while rotating;
   d) Removing the coated stent from said rotating bearing.

6. A process according to claim 5, wherein said stent is coated with a monolayer of said copolymer.

7. A process according to claim 5, wherein said stent is coated with a multilayer of said copolymer.

8. A process according to claims 5-7, wherein said horizontal rotating bearing is made of Teflon (R).

9. A process according to claims 5-8, wherein said horizontal rotating bearing can be rotated up to a maximum speed of 20rpm.

10. A process according to claims 5-9, wherein said copolymer is deposed on said stent by means of a solution of said copolymer.

11. A process according to claim 10, wherein an organic solvent is used in said solution.

12. A process according to claim 11, wherein dimethylacetamide is said solvent.

13. A process according to claims 10-12, wherein the concentration of said copolymer is comprised between 10 and 40% w/w.

Patentansprüche

1. Beschichtete endoluminale Metall-Gefäßprothese (Stent), dadurch charakterisiert, daß die endoluminale Gefäßprothese mit einem thermoplastischen Polycarbonaturethan beschichtet ist und daß die innere Oberfläche der polymerbeschichteten endoluminalen Gefäßprothese vollständig glatt ist, während die äußere Oberfläche perfekt zur Maschen-Struktur der endoluminalen Gefäßprothese paßt.

2. Endoluminale Gefäßprothese nach Anspruch 1, wobei Corethane® das Polycarbonaturethan ist.

3. Endoluminale Gefäßprothese nach den Ansprüchen 1 bis 2, wobei die endoluminale Gefäßprothese ausgewählt wird aus der Gruppe, die besteht aus Palmaz-, Palmaz-Schatz-, Gianturco-, Gianturco-Roubin-, Gianturco-Rosch-, Strecker-, Formgedächtnis-Stents.

4. Endoluminale Gefäßprothese nach den Ansprüche 1 bis 3, wobei ein Gianturco-Rosch die endoluminale Gefäßprothese ist.

5. Verfahren zum Beschichten einer endoluminalen Gefäßprothese nach den Ansprüchen 1 bis 4, wobei das Verfahren die Stufen umfaßt:

   a) Positionieren der endoluminalen Gefäßprothese in expandierter Konfiguration auf einer horizontalen rotierenden Halterung;
   b) Rotieren der Halterung;
   c) Abscheiden des Copolymeren auf der endoluminalen Gefäßprothese, während diese rotiert;
   d) Entfernen der beschichteten endoluminalen Gefäßprothese von der rotierenden Halterung.

6. Verfahren nach Anspruch 5, wobei die endoluminale Gefäßprothese mit einer Monoschicht des Copolymeren beschichtet ist.

7. Verfahren nach Anspruch 5, wobei die endoluminale Gefäßprothese mit einer Mehrfachschicht des Copolymeren beschichtet ist.

8. Verfahren nach den Ansprüchen 5 bis 7, wobei die horizontale rotierende Halterung aus Teflon (R) hergestellt ist.

9. Verfahren nach den Ansprüchen 5 bis 8, wobei die horizontale rotierende Halterung mit einer maximalen Geschwindigkeit von bis zu 20 Upm rotiert werden kann.

10. Verfahren nach den Ansprüchen 5 bis 9, wobei das Copolymer auf der endoluminalen Gefäßprothese mit Hilfe einer Lösung des Copolymeren abgeschieden wird.

11. Verfahren nach Anspruch 10, wobei ein organisches Lösungsmittel in der Lösung verwendet wird.

12. Verfahren nach Anspruch 11, wobei Dimethylacetamid als Lösungsmittel verwendet wird.

13. Verfahren nach den Ansprüchen 10 bis 12, wobei die Konzentration des Copolymeren zwischen 10 und 40 Gew.-% liegt.

Revendications

1. Un stent métallique revêtu, caractérisé en ce que ledit stent est revêtu d'un polycarbonate uréthane thermoplastique, et en ce que la surface intérieure du stent revêtu de polymère est totalement lisse, tandis que la surface extérieure s'adapte parfaitement à la structure maillée du stent.

2. Un stent selon la revendication 1, dans lequel le polycarbonate uréthane est du Coréthane®.

3. Un stent selon l'une quelconque des revendications 1 et 2, dans lequel ledit stent est choisi dans le groupe formé par les stents à mémoire de forme de Palmaz, de Palmaz-Schatz, de Gianturco, de Gianturco-Roubin, de Gianturco-Rosch, de Strecker.

4. Un stent selon l'une quelconque des revendications 1 à 3, dans lequel ledit stent est un stent de Gianturco-Rosch.

5. Un procédé pour revêtir un stent selon l'une quelconque des revendications 1 à 4, ledit procédé comprenant les opérations consistant :

   à) à placer le stent dans sa configuration dilatée sur un organe porteur rotatif horizontal ;
   b) à mettre en rotation ledit organe porteur ;
   c) à déposer le copolymère sur ledit stent pendant qu'il est en rotation ;
   d) à enlever le stent revêtu dudit organe porteur rotatif.

6. Un procédé selon la revendication 5, dans lequel ledit stent est revêtu d'une monocouche dudit copolymère.

7. Un procédé selon la revendication 5, dans lequel ledit stent est revêtu de plusieurs couches dudit copolymère.

8. Un procédé selon l'une quelconque des revendications 5 à 7, dans lequel ledit organe porteur rotatif horizontal est en Téflon®.

9. Un procédé selon l'une quelconque des revendications 5 à 8, dans lequel ledit organe porteur rotatif horizontal peut être animé d'une vitesse de rotation maximale non supérieure à 20 tours par minute.

10. Un procédé selon l'une quelconque des revendications 5 à 9, dans lequel ledit copolymère est déposé sur ledit stent au moyen d'une solution dudit copolymère.

11. Un procédé selon la revendication 10, dans lequel un solvant organique est utilisé dans ladite solution.

12. Un procédé selon la revendication 11, dans lequel ledit solvant est du diméthylacétamide.

13. Un procédé selon l'une quelconque des revendications 10 à 12, dans lequel la concentration dudit copolymère est comprise entre 10 est 40 % en poids.